

REMARKS

Pending Claims

Applicant's attorney acknowledges and apologizes for the error in identifying claims 13 and 14 as pending. These claims have been cancelled.

Claims 2, 4, 5, 12, 15-16, 25, 27, 34-37, 39, 40, 42 and 45-47 are now pending in the application. Applicants acknowledge that claims 34 and 35 are allowed.

Rejection under 35 USC §112, first paragraph

The withdrawal of this rejection acknowledged.

Rejection under 35 USC §103 in view of Atwal (US 5547966)

As discussed in the previous response, Atwal discloses aryl urea compounds which do not have the substituent "C(O)R_x" on a remote phenyl group or pyridinyl group (corresponding to L¹ of formula I herein and corresponding to R¹ of formula I of Atwal).

Atwal does not disclose any compounds where R¹ is pyridinyl and does not disclose any compounds where R¹ is substituted phenyl. Only two compounds (Examples 14 and 15) have R¹ as phenyl and these phenyl groups are unsubstituted. Only one compound (compound 17) has a substituent consistent with "C(O)R_x" herein and it is positioned on the "first phenyl group," not a remote ring.

Applicants submit the examiners obviousness analysis is inconsistent with that set forth by the Supreme Court in *KSR INTERNATIONAL CO. v. TELEFLEX INC. ET AL.* 548 U.S. 902 (2006) and that of the Federal Circuit in *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.* 492 F.3d 1350 (Fed. Cir. 2007) and *The Procter and Gamble Co. vs. TEVA Pharmaceuticals*, 566 F.3d 989 (Fed. Cir. 2009).

The examiner finds that "these compounds appear to have the same utility and in view of KSR, there is clear motivation to move the same substituent from one to the other phenyl. Especially so when Atwal discloses a broad genus..." and "So when the teaching is there that it can be substituted, one of skill in the art would be motivated to make different positional substituted compounds."

In KSR, the Supreme Court rejected the rigid application of the teaching, suggestion, or motivation test for combining known elements which limited the inquiry as to whether the combination is obvious. However, they made it clear

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness".

No articulated reasoning or rationale has been set forth as to why one skilled in the art would be motivated by the teachings of Atwal "to make different positional substituted compounds" necessary to arrive at the compounds claimed herein.

The Supreme Court further held,

"As is clear from cases such as Adams, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." "It can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does."

The examiner has not identified any reason that would have prompted a person of ordinary skill in the relevant field to select the substituents necessary to arrive at the claimed compounds.

The Supreme court also stated,

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

There is no evidence of a design need to make the substitutions necessary to arrive at the claimed compounds and there is no evidence there were a finite number of predictable solutions to arrive at the claimed compounds. In the absence of such evidence the substitutions necessary to arrive at the compounds claimed were not obvious to try. There were numerous substituents and locations to select from in substituting the compounds of Atwal and as discussed in the previous response, the substitutions necessary do not even fall within the broad generic disclosure of Atwal

in that compounds where R¹ is phenyl or pyridinyl are not substituted by “C(O)R_x”. The substitutions necessary to arrive at the claimed compounds clearly were not obvious to try. The absence of any substituents for R¹ conforming to the structure of “C(O)R_x” or chemical nature of “C(O)R_x” from this broad disclosure is conspicuous since this substituent appears at other locations on the compounds of Atwal.

The obviousness rejection based on structural similarity between the claimed compounds the compound of example 15 of Atwal requires a preliminary finding that one of ordinary skill in the art would have selected the compound of example 15 of Atwal as a lead compound for modification consistent with the holding in *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007). The preferred compounds defined at column 7 of Atwal encompass Examples 2, 3, 4, 5, 6, 10, 11, 12, 13, 14, 15, 17, and 18. No basis has been given for selecting example 15 as the lead.

In addition to the absence of evidence in selecting example 15 as the lead, no evidence has been presented showing one of ordinary skill in the art would have reason to attempt to modify the compound of Example 15 to make a compound claimed herein with a reasonable expectation that such a compound would retain the properties necessary for the treatment of ischemic conditions as disclosed by Atwal.

To maintain the rejection under 35 USC § 103, it is necessary to show that the prior art would have suggested making the specific molecular modifications necessary to Example 15 of Atwal to achieve a compound within the scope of the claims herein. See *The Procter and Gamble Co. vs. TEVA Pharmaceuticals*, 2008-1404, 1405 1406, May 13, 2009.

It remains necessary to identify some reason that would have led a chemist to incorporate the group “C(O)R_x” on a remote phenyl or pyridinyl group of R¹ although inconsistent with the teachings Atwal. See *The Procter and Gamble Co. vs. TEVA Pharmaceuticals*(supra). Applicants submit a modification inconsistent with the teachings of Atwal would not be routine and is unobvious, such that the rejection under 35 USC § 103 should be withdrawn.

The patent at issue in *The Procter and Gamble Co. vs. TEVA Pharmaceuticals* (supra) claimed a positional isomer (risedronate) of a prior art compound. The Federal Circuit found there was no credible evidence it would have been routine to move the position of the substituent of the prior art compound and that the evidence of record did not establish that it would have been obvious to move the substituent of the prior art compound to the position necessary to create risedronate.

Similarly, there is no evidence of record in this application that placing the substituent $-C(O)R_x$ on a remote ring (L^1 herein) would have been routine or that it would have been obvious to modify the compounds of Atwal to create the compounds claimed herein. In the absence of such evidence, Applicants submit the rejection under 35 USC 103 should be withdrawn.

Double Patenting

The rejection for obviousness type double patenting based on claims 1 and 21 of US patent No. 7,371,763 and claims 22 and 23 of copending serial number 11/932269 should be withdrawn in that these claims exclude the subject matter claimed herein based on the proviso that

“where B, B' or B'' is $-L(ML^1)_n$, L^1 is not substituted by the substituents $-C(O)R^a$, $-C(NR^b)R^b$, $-C(O)NR^aR^b$ and $-SO_2R^a$ wherein each R^a and R^b are independently hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O,”

The subject matter of claims 1 and 21 of US patent No. 7,371,763 and claims 22 and 23 of copending serial number 11/932269 patent would not render the subject matter claimed herein obvious in view of the proviso above.

Based on the above remarks, Applicants respectfully request reconsideration of the objections and rejections identified above.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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